RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004220409 A1 20041104 US 2003-468628 20030820

PRIORITY APPLN. INFO.: US 2001-270048P P 20010220
US 2001-271788P P 20010227
WO 2002-US5390 W 20020220

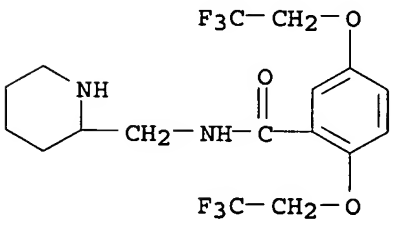
OTHER SOURCE(S): CASREACT 137:201232; MARPAT 137:201232

AB An improved, highly efficient method for the preparation of flecainide acetate or other pharmaceutically acceptable salts of flecainide involves preparing the staring material 1,4-bis(2,2,2-trifluoroethoxy)benzene in high yields by reacting 4-fluoro-1-bromobenzene with F3CCH2OH in the presence of a base and a copper-containing catalyst.

IT **54143-55-4P**, Flecainide
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(flecainide synthesis)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:861473 CAPLUS

DOCUMENT NUMBER: 134:32972

TITLE: Porous drug matrixes containing polymers and sugars and methods of their manufacture

INVENTOR(S): Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg

PATENT ASSIGNEE(S): Acusphere, Inc., USA

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072827	A2	20001207	WO 2000-US14578	20000525 <--
WO 2000072827	A3	20010125		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6395300	B1	20020528	US 1999-433486	19991104 <--
CA 2371836	AA	20001207	CA 2000-2371836	20000525 <--
EP 1180020	A2	20020220	EP 2000-939365	20000525 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010984	A	20020430	BR 2000-10984	20000525 <--

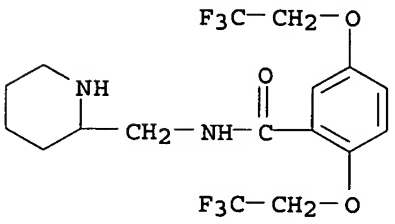
JP 2003500438	T2	20030107	JP 2000-620939		20000525
NZ 516083	A	20030829	NZ 2000-516083		20000525
AU 768022	B2	20031127	AU 2000-54459		20000525
US 2002041896	A1	20020411	US 2001-798824		20010302 <--
US 6610317	B2	20030826			
NO 2001005753	A	20020128	NO 2001-5753		20011126 <--
ZA 2001010347	A	20030730	ZA 2001-10347		20011218
PRIORITY APPLN. INFO.:			US 1999-136323P	P	19990527
			US 1999-158659P	P	19991008
			US 1999-433486	A	19991104
			US 2000-186310P	P	20000302
			WO 2000-US14578	W	20000525

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution was prepared by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

IT **54143-55-4**, Flecainide
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); **PROC (Process)**; USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

RN 54143-55-4 CAPLUS

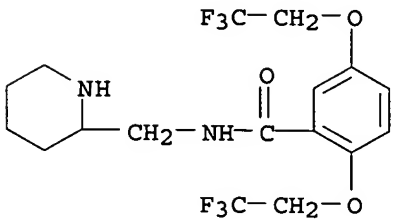
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



L16 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2000:40090 CAPLUS
DOCUMENT NUMBER:	132:103844
TITLE:	Extractableness of relevant toxicological compounds with 1-chlorbutane
AUTHOR(S):	Demme, U.; Becker, J.; Bussemas, H.; Daldrup, Th.; Erdmann, F.; Erkens, M.; Iten, P. X.; Magerl, H.; Von Meyer, L.; Teske, J.; Weinmann, W.; Weller, J. P.
CORPORATE SOURCE:	Institut fur Rechtsmedizin Friedrich-Schiller-

Universitat, Jena, D-07740, Germany
SOURCE: GTFCh-Symposium: Nachweis Berauschender Mittel im Strassenverkehr -- Forensische Aspekte der Toxischen Praeparation von Lebensmitteln, Beitraegezum Symposium der Gesellschaft fuer Toxikologische und Forensische Chemie, 11th, Mosbach, Germany, Apr. 22-24, 1999 (1999), 213-218. Editor(s): Pragst, Fritz; Aderjan, Rolf. Verlag Dr. Dieter Helm: Heppenheim, Germany.
CODEN: 68NJAK
DOCUMENT TYPE: Conference
LANGUAGE: German
AB Extractability of 160 active components was tested in aqueous solution and blood serum (phosphate-buffer, pH = 9) with 1-chlorobutane in interlab. tests. Extraction yields were determined and partial compared with values from literature.
IT **54143-55-4**, Flecainide
RL: PEP (Physical, engineering or chemical process); **PROC (Process)**
(extractableness of relevant toxicol. compds. from water and blood serum with 1-chlorbutane)
RN 54143-55-4 CAPLUS
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:64776 CAPLUS
DOCUMENT NUMBER: 130:124996
TITLE: Process and a novel intermediate for the preparation of Flecainide
INVENTOR(S): Gutman, Arie L.; Nisnevich, Genady; Shkolnik, Eleonora; Zaltzman, Igor
PATENT ASSIGNEE(S): Finetech Ltd., Israel
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902498	A1	19990121	WO 1998-IL315	19980707 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
IL 121288	A1	20001031	IL 1997-121288	19970711 <--
AU 9881265	A1	19990208	AU 1998-81265	19980707 <--
EP 996616	A1	20000503	EP 1998-931000	19980707 <--
EP 996616	B1	20040512		
R: ES, FR, IT				

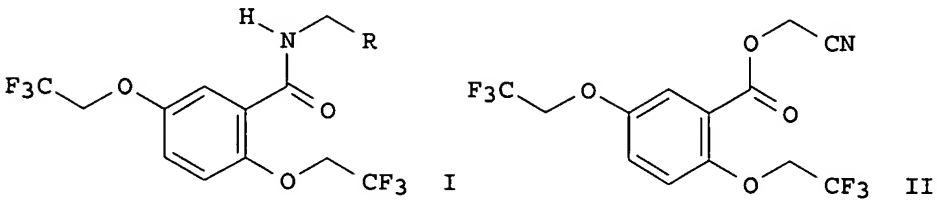
US 6316627	B1	20011113	US 1999-422931	19991021	<--
US 6538138	B1	20030325	US 2000-462418	20000403	
US 2002133013	A1	20020919	US 2001-911366	20010723	<--
US 6593486	B2	20030715			

PRIORITY APPLN. INFO.:

IL 1997-121288	A	19970711
IL 1997-120715	A	19970421
WO 1998-IL187	A2	19980420
WO 1998-IL315	W	19980707
US 1999-422931	A1	19991021

OTHER SOURCE(S): CASREACT 130:124996; MARPAT 130:124996

GI



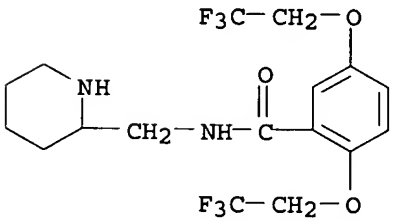
I II

AB The title compds. [I; R = 2-piperidyl, 2-pyridyl] and their pharmaceutically acceptable salts, were prepared by a) reacting 2,5-bis(2,2,2,-trifluoroethoxy)**benzoic** acid or its salt with a haloacetonitrile XCH2CN (wherein X = Cl, Br, I) if necessary in the presence of an inorg. or organic base, b) reacting the cyanomethyl ester II with an amine RCH2NH2; c) converting the compound I to its pharmaceutically acceptable salt.

IT **54143-55-4P**, Flecainide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(process and a novel intermediate for the preparation of Flecainide)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:293427 CAPLUS

DOCUMENT NUMBER: 129:8597

TITLE: Embedding and encapsulation of controlled release particles

INVENTOR(S): Van Lengerich, Bernhard H.

PATENT ASSIGNEE(S): Van Lengerich, Bernhard H., USA

SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

=> d l13 1-4 ibib abs hitstr

L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:238745 CAPLUS
DOCUMENT NUMBER: 142:297883
TITLE: A novel process for preparation of antiarrhythmic flecainide and its intermediates
INVENTOR(S): Wang, Zhi-Xian; Li, Yuanqiang; Guntoori, Bhaskar Reddy
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005059825	A1	20050317	US 2003-663836	20030917
PRIORITY APPLN. INFO.:			US 2003-663836	20030917

OTHER SOURCE(S): CASREACT 142:297883; MARPAT 142:297883
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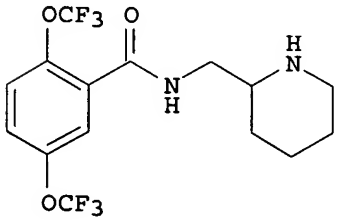
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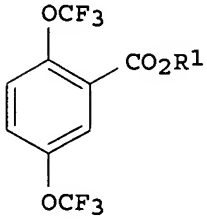
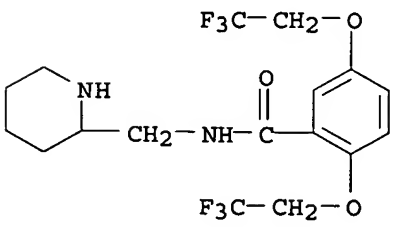

II

AB The invention relates to a process for preparation of antiarrhythmic flecainide (I) and its intermediates of formula II (R1 is H, alkali metal, or alkyl). Flecainide (I) was prepared via amidation of II (R1 = Me) by 2-(aminomethyl)piperidine with a yield of 85%. This new process is an inexpensive and efficient process for manufacture of flecainide and its intermediates.

IT **54143-55-4P**, Flecainide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(novel process for preparation of antiarrhythmic flecainide and its intermediates)

RN 54143-55-4 CAPLUS
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:658065 CAPLUS
DOCUMENT NUMBER: 137:201232
TITLE: Flecainide synthesis

INVENTOR(S): McDaniel, William C.; Radhakrishnan, Jayaramaiyer; Janicki, Slawomir J.
PATENT ASSIGNEE(S): Narchem Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066413	A1	20020829	WO 2002-US5390	20020220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004220409	A1	20041104	US 2003-468628	20030820

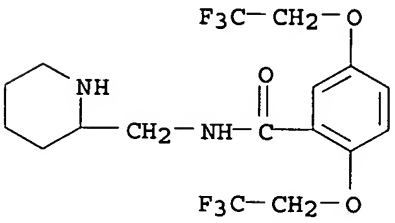
PRIORITY APPLN. INFO.:
US 2001-270048P P 20010220
US 2001-271788P P 20010227
WO 2002-US5390 W 20020220

OTHER SOURCE(S): CASREACT 137:201232; MARPAT 137:201232

AB An improved, highly efficient method for the preparation of flecainide acetate or other pharmaceutically acceptable salts of flecainide involves preparing the staring material 1,4-bis(2,2,2-trifluoroethoxy)benzene in high yields by reacting 4-fluoro-1-bromobenzene with F3CCH2OH in the presence of a base and a copper-containing catalyst.

IT **54143-55-4P**, Flecainide
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(flecainide synthesis)

RN 54143-55-4 CAPLUS
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

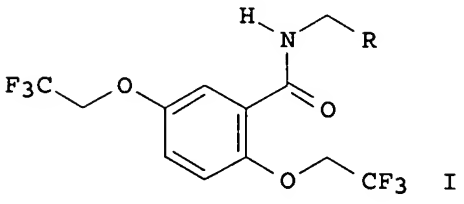
L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:64776 CAPLUS
DOCUMENT NUMBER: 130:124996
TITLE: Process and a novel intermediate for the preparation of Flecainide
INVENTOR(S): Gutman, Arie L.; Nisnevich, Genady; Shkolnik, Eleonora; Zaltzman, Igor
PATENT ASSIGNEE(S): Finetech Ltd., Israel
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902498	A1	19990121	WO 1998-IL315	19980707
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
IL 121288	A1	20001031	IL 1997-121288	19970711
AU 9881265	A1	19990208	AU 1998-81265	19980707
EP 996616	A1	20000503	EP 1998-931000	19980707
EP 996616	B1	20040512		
R: ES, FR, IT				
US 6316627	B1	20011113	US 1999-422931	19991021
US 6538138	B1	20030325	US 2000-462418	20000403
US 2002133013	A1	20020919	US 2001-911366	20010723
US 6593486	B2	20030715		

PRIORITY APPLN. INFO.:	IL 1997-121288	A	19970711
	IL 1997-120715	A	19970421
	WO 1998-IL187	A2	19980420
	WO 1998-IL315	W	19980707
	US 1999-422931	A1	19991021

OTHER SOURCE(S): CASREACT 130:124996; MARPAT 130:124996

GI



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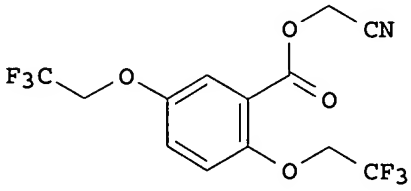


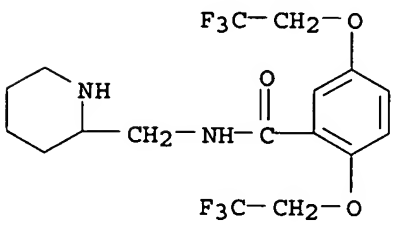
II

AB The title compds. [I; R = 2-piperidyl, 2-pyridyl] and their pharmaceutically acceptable salts, were prepared by a) reacting 2,5-bis(2,2,2,-trifluoroethoxy)**benzoic acid** or its salt with a haloacetonitrile XCH2CN (wherein X = Cl, Br, I) if necessary in the presence of an inorg. or organic base, b) reacting the cyanomethyl ester II with an amine RCH2NH2; c) converting the compound I to its pharmaceutically acceptable salt.

IT **54143-55-4P**, Flecainide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(process and a novel intermediate for the preparation of Flecainide)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:122069 CAPLUS
DOCUMENT NUMBER: 114:122069
TITLE: Preparation of 2,5-bis(2,2,2-trifluoroethoxy-N-(2-piperidinylmethyl)benzamide acetate
INVENTOR(S): Rubio Zurita, Pelayo; Cirera Dotti, Xavier; Irurre Perez, Jose
PATENT ASSIGNEE(S): Laboratorios Rubio S. A., Spain
SOURCE: Span., 7 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2007802	A6	19890701	ES 1988-830	19880318
PRIORITY APPLN. INFO.:			ES 1988-830	19880318
OTHER SOURCE(S):	MARPAT 114:122069			

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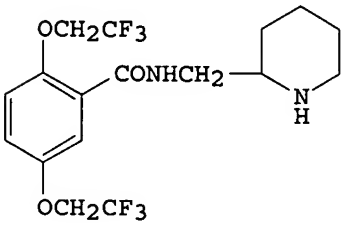

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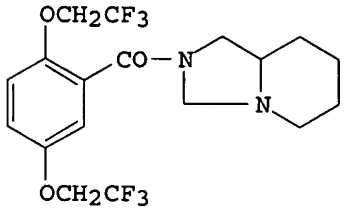
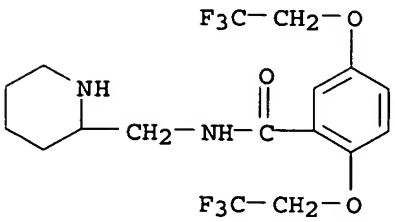


IV

AB The title compound (I.HOAc) is prepared by reaction of an activated derivative of 2,5-bis(2,2,2-trifluoroethoxy)**benzoic acid** (II) with 2-azaindolizidine (III) to give the heterocyclic amide IV as the HCl salt, which is selectively hydrolyzed to I followed by salification with glacial HOAc. Thus, II was treated with SOCl2 at room temperature to give the acid chloride, which reacted with distilled III in CH2Cl2 to give 97% IV.HCl. The latter was hydrolyzed with aqueous HCl in EtOH to give 81% I, which was treated with HOAc in Me2CHOH.

IT **54143-55-4P**, Flecainide
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of, from bis(trifluoroethoxy)**benzoic acid** and azaindolazidine)

RN 54143-55-4 CAPLUS
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



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AU 9749915	A1	19980522	AU 1997-49915		19971027 <--
AU 744156	B2	20020214			
EP 935523	A1	19990818	EP 1997-912825		19971027 <--
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JP 2002511777	T2	20020416	JP 1998-520558		19971027 <--
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AT 277739	E	20041015	AT 1997-912825		19971027
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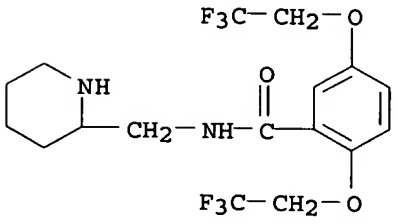
			US 1997-52717P	P	19970716
			EP 1997-912825	A3	19971027
			WO 1997-US18984	W	19971027

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temperature of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixture The mixture is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

IT **54143-55-4**, Flecainide
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); **PROC (Process)**; USES (Uses)
(embedding and encapsulation of controlled release particles)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:122069 CAPLUS
DOCUMENT NUMBER: 114:122069

TITLE: Preparation of 2,5-bis(2,2,2-trifluoroethoxy-N-(2-piperidinylmethyl)benzamide acetate

INVENTOR(S): Rubio Zurita, Pelayo; Cirera Dotti, Xavier; Irurre Perez, Jose

PATENT ASSIGNEE(S): Laboratorios Rubio S. A., Spain

SOURCE: Span., 7 pp.
CODEN: SPXXAD

DOCUMENT TYPE: Patent

LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2007802	A6	19890701	ES 1988-830	19880318 <--

PRIORITY APPLN. INFO.: ES 1988-830 19880318

OTHER SOURCE(S): MARPAT 114:122069

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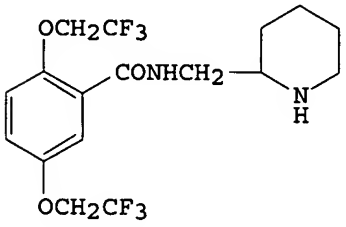

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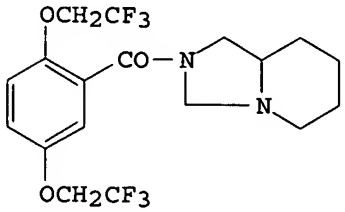


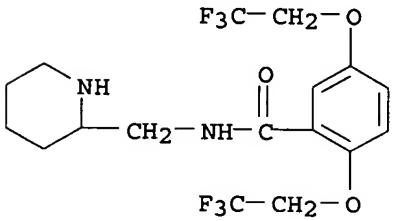
IV

AB The title compound (I.HOAc) is prepared by reaction of an activated derivative of 2,5-bis(2,2,2-trifluoroethoxy)**benzoic** acid (II) with 2-azaindolizidine (III) to give the heterocyclic amide IV as the HCl salt, which is selectively hydrolyzed to I followed by salification with glacial HOAc. Thus, II was treated with SOCl2 at room temperature to give the acid chloride, which reacted with distilled III in CH2Cl2 to give 97% IV.HCl. The latter was hydrolyzed with aqueous HCl in EtOH to give 81% I, which was treated with HOAc in Me2CHOH.

IT **54143-55-4P**, Flecainide
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of, from bis(trifluoroethoxy)**benzoic** acid and azaindolazidine)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



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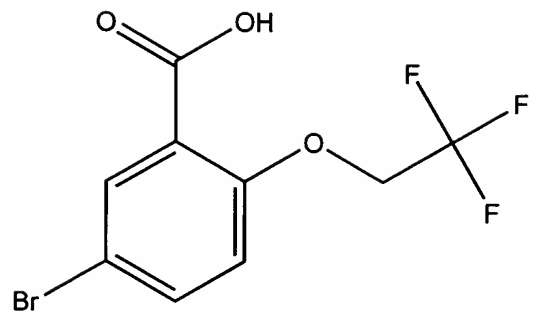

5-bromo-2-(2,2,2-trifluoroethoxy)benzoic acid

http://www.cas.org/infopolicy.html

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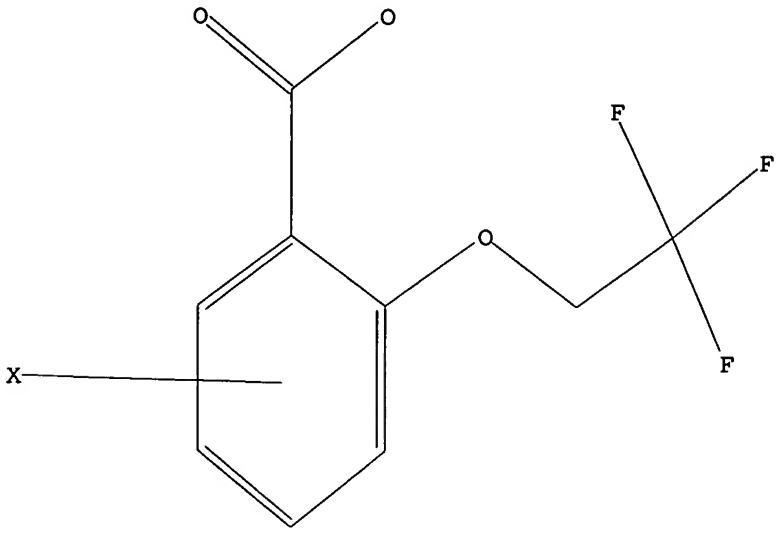
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

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SEARCH TIME: 00.00.01

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BATCH **COMPLETE**
PROJECTED ITERATIONS: 20335 TO 24345
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L3 1 L2

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L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:315042 CAPLUS
DOCUMENT NUMBER: 126:293352
TITLE: Preparation of benzimidazoles for the prevention and/or the treatment of bone diseases

INVENTOR(S): Oku, Teruo; Kawai, Yoshio; Yatabe, Takumi; Sato, Shigeki; Yamazaki, Hitoshi; Kayakiri, Natsuko; Yoshihara, Kousei
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9710219	A1	19970320	WO 1996-JP2530	19960905
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 863881	A1	19980916	EP 1996-929540	19960905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11513364	T2	19991116	JP 1996-511824	19960905
PRIORITY APPLN. INFO.:			GB 1995-18552 A	19950911
			WO 1996-JP2530 W	19960905

OTHER SOURCE(S): MARPAT 126:293352
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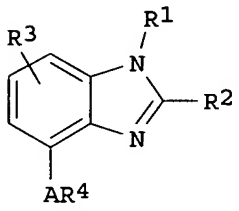


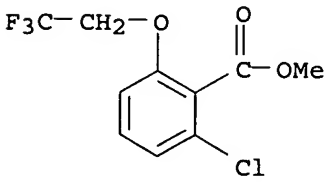
I

AB The title compds. [I; R1 = acyl, (un)substituted lower alkenyl, lower alkyl; R2 = H, lower alkyl, lower alkoxy, etc.; R1R2 = lower alkylene, lower alkenylene (may include O, S, NH, N-alkyl); R3 = H, halo; R4 = (un)substituted heterocyclyl, aryl; A = CONR9, N(R10)CO (wherein R9, R10 = H, (un)substituted lower alkyl)], and their pharmaceutically acceptable salts, inhibitors of bone resorption and bone metabolism, were prepared Thus, hydrogenation of 1,2-dimethyl-4-nitro-1H-benzimidazole over 10% Pd/C in MeOH followed by reaction of the resulting 4-amino-1,2-dimethyl-1H-benzimidazole with 2,6-dichlorobenzoyl chloride in the presence of Et3N in ethylene chloride afforded I [R1, R2 = Me; R3 = H; R4 = 2,6-Cl2C6H3; A = NHCO]. Compds. I are effective at 0.1-1000 mg/body/day.

IT **189045-94-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzimidazoles for the prevention and/or the treatment of bone diseases)

RN 189045-94-1 CAPLUS

CN Benzoic acid, 2-chloro-6-(2,2,2-trifluoroethoxy)-, methyl ester (9CI) (CA INDEX NAME)



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REGlstRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

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FULL SCREEN SEARCH COMPLETED - 21898 TO ITERATE

100.0% PROCESSED 21898 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

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L5 3 L4

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L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:315042 CAPLUS
DOCUMENT NUMBER: 126:293352
TITLE: Preparation of benzimidazoles for the prevention and/or the treatment of bone diseases
INVENTOR(S): Oku, Teruo; Kawai, Yoshio; Yatabe, Takumi; Sato, Shigeki; Yamazaki, Hitoshi; Kayakiri, Natsuko; Yoshihara, Kousei
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9710219	A1	19970320	WO 1996-JP2530		19960905
W: JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 863881	A1	19980916	EP 1996-929540		19960905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 11513364	T2	19991116	JP 1996-511824		19960905
PRIORITY APPLN. INFO.:			GB 1995-18552	A	19950911
			WO 1996-JP2530	W	19960905

OTHER SOURCE(S): MARPAT 126:293352
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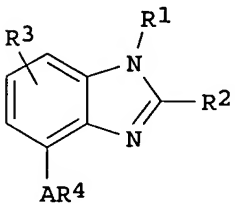


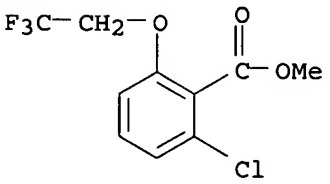
I

AB The title compds. [I; R1 = acyl, (un)substituted lower alkenyl, lower alkyl; R2 = H, lower alkyl, lower alkoxy, etc.; R1R2 = lower alkylene, lower alkenylene (may include O, S, NH, N-alkyl); R3 = H, halo; R4 = (un)substituted heterocyclyl, aryl; A = CONR9, N(R10)CO (wherein R9, R10 = H, (un)substituted lower alkyl)], and their pharmaceutically acceptable salts, inhibitors of bone resorption and bone metabolism, were prepared Thus, hydrogenation of 1,2-dimethyl-4-nitro-1H-benzimidazole over 10% Pd/C in MeOH followed by reaction of the resulting 4-amino-1,2-dimethyl-1H-

benzimidazole with 2,6-dichlorobenzoyl chloride in the presence of Et3N in ethylene chloride afforded I [R1, R2 = Me; R3 = H; R4 = 2,6-Cl2C6H3; A = NHCO]. Compds. I are effective at 0.1-1000 mg/body/day.

IT **189045-94-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzimidazoles for the prevention and/or the treatment of bone diseases)

RN 189045-94-1 CAPLUS
CN Benzoic acid, 2-chloro-6-(2,2,2-trifluoroethoxy)-, methyl ester (9CI) (CA INDEX NAME)



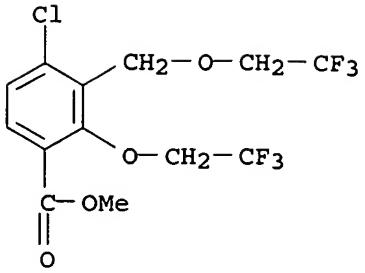
L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:969484 CAPLUS
DOCUMENT NUMBER: 124:3056
TITLE: Preparation of isoxazole as pesticides.
INVENTOR(S): Cain, Paul Alfred; Chou, David; Herman, Nancy D.; Gant, Daniel B.; Shoberu, Karoline A.
PATENT ASSIGNEE(S): Rhone Poulenc Agrochimie, Fr.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9522904	A1	19950831	WO 1995-EP617		19950221
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9517585	A1	19950911	AU 1995-17585		19950221
PRIORITY APPLN. INFO.:			US 1994-201583	A	19940225
			WO 1995-EP617	W	19950221

OTHER SOURCE(S): MARPAT 124:3056
GI For diagram(s), see printed CA Issue.
AB The isoxazoles I [R=H,alkoxycarbonyl, etc.;A=C(O)W and B=R1 or A=C(O)R1 and B=W; W=(un)substituted Ph;R1=(cyclo)alkyl or (un)substituted Ph] are acaricides, insecticides and nematocides. Thus, 4-[4-bromo-2-(2,2,3,3,3-pentafluoropropoxymethyl)benzoyl]-5-cyclopropylisoxazole (preparation given) controlled the two-spotted spider mite.

IT **171187-94-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate in preparation of isoxazole pesticides)

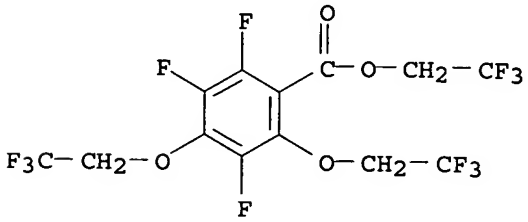
RN 171187-94-3 CAPLUS
CN Benzoic acid, 4-chloro-2-(2,2,2-trifluoroethoxy)-3-[(2,2,2-trifluoroethoxy)methyl]-, methyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:903124 CAPLUS
DOCUMENT NUMBER: 124:116744
TITLE: Synthesis of Polyfluoro Aromatic Ethers: A Facile Route Using Polyfluoroalkoxides Generated from Carbonyl and Trimethysilyl Compounds
AUTHOR(S): Nishida, Masakazu; Vij, Ashwani; Kirchmeier, Robert L.; Shreeve, Jean'ne M.
CORPORATE SOURCE: Department of Chemistry, University of Idaho, Moscow, ID, 83844, USA
SOURCE: Inorganic Chemistry (1995), 34(24), 6085-92
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:116744

AB The polyfluoro aromatic ethers C6F5CH2ORF [RF = CF3, C2F5, CH2CF3, CF(CF3)2, C(CF3)3, C(CF3)2C6F5, C(CF3)2OCH2CF3, C(C6F5)2CF3], 4-CF3CH2OC6F4CH2OCH2CF3, and C6F5CH2OCF2CF2OCH2C6F5 were synthesized from C6F5CH2Br in the presence of CsF by reaction with the perfluoro carbonyl compds. COF2, CF3C(O)F, C6F5COF, (C6F5)2CO, (CF3)2CO, and (COF)2; reaction with polyfluoro siloxanes CF3CH2OSi(CH3)3 and C6F5OSi(CH3)3; or reaction with polyfluoroalkoxides generated from the fluorinated silanes CF3Si(CH3)3, C6F5Si(CH3)3, and CF3CH2OSi(CH3)3 reacting with the carbonyl compds. listed above. Single-crystal X-ray anal. of C6F5CH2OC(C6F5)2CF3 was reported. Reactivities of the carbonyl substrates and the silicon-containing reagents are discussed as a function of the alkyl (aryl) substituents present.

IT **172976-33-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of polyfluoro aromatic ethers)
RN 172976-33-9 CAPLUS
CN Benzoic acid, 2,3,5-trifluoro-4,6-bis(2,2,2-trifluoroethoxy)-, 2,2,2-trifluoroethyl ester (9CI) (CA INDEX NAME)



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http://www.cas.org/ONLINE/UG/regprops.html

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L7            1 FLECAINIDE/CN

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L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   54143-55-4  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI)
     (CA INDEX NAME)
OTHER NAMES:
CN   (±)-Flecainide
CN   Flecaine
CN   Flecainide
FS   3D CONCORD
DR   99495-87-1
MF   C17 H20 F6 N2 O3
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN,
       DDFU, DIOGENES, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH,
       IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH,
       SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   WHO
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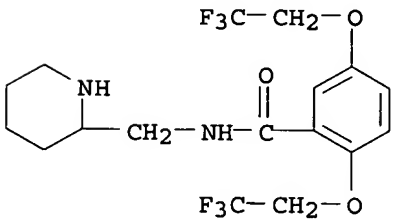


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             541 REFERENCES IN FILE CA (1907 TO DATE)
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             541 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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               S L1

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     FILE 'CAPLUS' ENTERED AT 15:54:04 ON 28 NOV 2005
L5             3 S L4 FULL

     FILE 'CAPLUS' ENTERED AT 16:22:19 ON 28 NOV 2005

     FILE 'REGISTRY' ENTERED AT 16:22:32 ON 28 NOV 2005
L6             0 S FLECANIDE/CN
L7             1 S FLECAINIDE/CN

     FILE 'CAPLUS' ENTERED AT 16:23:39 ON 28 NOV 2005
L8            13 S 54143-55-4/PREP
L9            38 S 54143-55-4/PROC
L10            0 S 54143-55-4/PUR
L11           51 S L8 OR L9
L12            0 S L11 AND HALOBENZOIC ACID
L13            4 S L11 AND BENZOIC ACID
L14            0 S 1-4 IBIB ABS HITSTR

=> s l11 and py<2003
      22790424 PY<2003
L15           45 L11 AND PY<2003

=> s l15 and  benzo?
        527879 BENZO?
L16            6 L15 AND  BENZO?

=> d  1-6 ibib abs hitstr

L16  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2002:658065  CAPLUS
DOCUMENT NUMBER:          137:201232
TITLE:                    Flecainide synthesis
INVENTOR(S):              McDaniel, William C.; Radhakrishnan, Jayaramaiyer;
                          Janicki, Slawomir J.
PATENT ASSIGNEE(S):       Narchem Corporation, USA
SOURCE:                   PCT Int. Appl., 24 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE         APPLICATION NO.          DATE
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     WO 2002066413         A1    20020829     WO 2002-US5390           20020220 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
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